

CLAIMS

1. Method for the selection, identification or characterization of compounds which can modulate reverse cholesterol transport, which comprises :
 - contacting a test compound with a nucleic acid construct comprising, as the only LRH-1 response element, at least one copy of the LRH-1 response element of the promoter of the human apolipoprotein AI gene containing the following sequence (SEQ ID NO : 1): 5'-CTGATCCTTGAAC-3', and
 - determining the possible binding of said test compound to the response element.
2. Method according to claim 1, characterized in that the contact is carried out in the presence of the exogenous LRH-1 receptor or a functional equivalent thereof, and in that one determines the possible binding of said test compound to the LRH-1 response element and/or to the complex formed by the binding of LRH-1 to its response element.
3. Method for the selection, identification or characterization of compounds which can modulate reverse cholesterol transport, which comprises :
 - contacting a test compound with a host cell containing a reporter gene expression cassette, said cassette comprising a reporter gene placed under the control of a promoter comprising, as the only LRH-1 response element, at least one copy of the LRH-1 response element of the promoter of the human apolipoprotein AI gene containing the following sequence (SEQ ID NO : 1): 5'-CTGATCCTTGAAC-3', and
 - determining the effect of the presence of the test compound on the binding of LRH-1 to the response element or on the expression of the reporter gene.
4. Method according to claim 3, characterized in that the host cell comprises an exogenous LRH-1 receptor or a functional equivalent thereof.
5. Method according to either one of claims 3 or 4, characterized in that the host cell comprises a ligand of LRH-1.

6. Method according to any one of claims 3 to 5 comprising determining the level of expression of the reporter gene in the presence of the test compound and in the absence of said compound, an increase or a decrease in the level of reporter gene expression indicating the ability of the test compound to modulate reverse cholesterol transport.
7. Method according to any one of claims 3 to 6, characterized in that the host cell is a mammalian cell.
8. Method according to claim 7, characterized in that the mammalian cell is a human cell.
9. Method according to any one of claims 3 to 8, characterized in that the reporter gene is a gene coding for a product whose activity or presence in biological extracts can be measured, in particular one of the genes coding for luciferase, secreted alkaline phosphatase, galactosidase or lactamase.
10. Method according to any one of claims 3 to 9, characterized in that the promoter is selected in the group consisting of the HSV-TK promoter, the CMV immediate early promoter, the PGK promoter, the promoter of the gene coding for human apolipoprotein AI and the SV40 promoter.
11. Method according to any one of claims 1 to 10, characterized in that one or more compounds are tested, as a mixture or separately.
12. Method according to any one of claims 1 to 11, characterized in that the test compound is a combinatorial library.
13. Method according to claim 12, characterized in that the test compound is a clone or a library of nucleic acid clones coding for one or more DNA-binding polypeptide(s).
14. Method according to any one of the previous claims, characterized in that contact is carried out in a multiwell plate.

15. Method according to any one of the previous claims, additionally comprising a comparison of the possible effects determined by said method with the possible effects determined by a method carried out in the same conditions but with a nucleic acid construct containing at least one mutated copy of the LRH-1 response element of the promoter of the human apolipoprotein AI gene, containing the following sequence (SEQ ID NO : 1): 5'-CTGATCCTTGAAC-3',
said mutant copy essentially being unable to bind the LRH-1 receptor.
16. Method according to any one of the previous claims, for the selection, identification or characterization of compounds which can increase reverse cholesterol transport.
17. Method according to any one of claims 1 to 15, for the selection, identification or characterization of compounds which can modulate the activity of HDL.
18. Method according to any one of claims 1 to 15, for the selection, identification or characterization of compounds which can modulate the expression of apolipoprotein AI.
19. Use of a compound which can modulate the binding of LRH-1 and/or its cofactors to the response element of the promoter of the human apolipoprotein gene or a functional variant thereof, for preparing a composition intended to modulate reverse cholesterol transport.
20. Use of a compound increasing the binding of LRH-1 and/or its cofactors to the sequence SEQ ID NO : 1 or a functional variant thereof, for preparing a composition intended to increase reverse cholesterol transport.
21. Use of a compound modulating the binding of LRH-1 and/or its cofactors to the sequence SEQ ID NO : 1 or a functional variant thereof, for preparing a composition intended to modulate the activity of HDL.
22. Use of a compound increasing the binding of LRH-1 and/or its cofactors to the sequence SEQ ID NO : 1 or a functional variant thereof, for preparing a composition intended to increase the activity of HDL.

23. Use of a compound modulating the binding of LRH-1 and/or its cofactors to the sequence SEQ ID NO : 1 or a functional variant thereof, for preparing a composition intended to modulate the expression of ApoAI.
24. Use of a compound increasing the effect of LRH-1 and/or its cofactors on the transcription of the human apolipoprotein AI gene for preparing a composition intended to modulate reverse cholesterol transport.
25. Use according to any one of claims 19 to 24 in which said compound is a biological compound or a chemical compound.
26. Use according to any one of claims 19 to 24, characterized in that the compound is a nuclear factor or a cofactor.
27. Use according to any one of claims 19 to 24, characterized in that the compound is a clone expressing one or more DNA-binding polypeptide(s).
28. Use according to any one of claims 19 to 24, characterized in that the compound is a compound which is selected, identified or characterized according to any one of claims 1 to 18.
29. Nucleic acid fragment characterized by the following sequence (SEQ ID NO : 1):
5'-CTGATCCTTGAAC-3'.
30. Expression cassette comprising at least one copy of the nucleic acid fragment according to claim 29, and a promoter, selected from among the CMV immediate early promoter and the PGK promoter, associated with a reporter gene placed under the control of said promoter.
31. Use of a cassette according to claim 30, for *in vitro* screening of compounds which can modulate the activity of HDL.
32. Pharmaceutical composition comprising a compound which is selected, identified or

characterized according to any one of claims 1 to 18.